DEPARTMENT OF HEALTH AND HUMAN SERVICES

and

CENTERS FOR DISEASE CONTROL AND PREVENTION

convene the

ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS

Atlanta, Georgia
June 8-9, 2005

RECORD OF THE PROCEEDINGS

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Draft Minutes of the Meeting

The Department of Health and Human Services (HHS) and the Centers for Disease Control and Prevention (CDC) convened a meeting of the Advisory Council for the Elimination of Tuberculosis (ACET). The proceedings were held on June 8-9, 2005 at CDC's Corporate Square Facility, Building 8, in Atlanta, Georgia.

Opening Session

Dr. Masae Kawamura, the ACET Chair, called the meeting to order at 8:40 a.m. on June 8, 2005. She welcomed the attendees to the proceedings and opened the floor for introductions. The list of participants is appended to the minutes as Attachment 1.

Dr. Ronald Valdiserri, the ACET Executive Secretary, made several announcements. ACET is a federal advisory committee that provides advice to the HHS Secretary and CDC Director on the important issue of TB elimination in the United States. ACET meetings are open to the public and all comments made during the proceedings are a matter of public record. Members should be mindful of potential conflicts of interest identified by the CDC Committee Management Office and recuse themselves from voting or participating in these discussions.

The terms of Dr. Jeffrey Douglas, Ms. Teresa Garrett and Ms. Eileen Napolitano will expire in June 2005, but these members will be invited to attend the next ACET meeting and receive official recognition of their diligent efforts and dedication to TB elimination.

TB as a Health Disparity

HHS Perspective. Dr. Garth Graham, the Deputy Assistant Secretary for Minority Health in the HHS Office of Minority Health (OMH), described the role and function of OMH. OMH's mission is to improve the health of racial/ethnic minority populations by developing health policies and programs that will assist in eliminating health disparities. Estimates show that minorities will represent ~50% of the general population by 2040. OMH advises HHS on public health policies and programs that address health disparities and impact racial/ethnic minority groups. OMH fulfills its role through several internal and external partners, including all HHS operating divisions, other public health agencies at federal, state and local levels, faith-based organizations (FBOs), community-based organizations (CBOs), academic institutions, industry and businesses.

Several actions were taken to develop key policies, coordinate activities and establish priorities within OMH and throughout HHS. The HHS Council on Health Disparities (HHS Council) is represented by senior leadership from all HHS agencies and was established to design HHS-wide strategies, address budgetary issues and focus on other areas related to health disparities. At its most recent meeting, the HHS Council discussed the need to address diseases that HHS has not traditionally viewed as health disparities, particularly the growing epidemic of TB and multidrug-resistant TB (MDR-TB) in Hmong refugees. The HHS Council formed a number of subcommittees to focus on priority issues, such as cultural competency and workforce diversity. The HHS health disparities strategic framework was designed to specifically address diseases that disproportionately affect minority populations, such as obesity in African Americans.

Dr. Graham encouraged ACET to educate OMH and HHS on the need to address TB as a health disparity and identify next steps to advance this effort. Most notably, TB disproportionately affects minority populations and the disease also plays a major role in the overall public health system. He clarified that HHS focuses on pertinent problems affecting minority communities and does not address health disparities from a "list." Collaboration with and education by ACET will assist OMH in recognizing TB as a priority in health disparities and developing practical strategies to address all diseases throughout HHS that impact racial/ethnic groups.

Dr. Graham also emphasized the need to design culturally-appropriate approaches at the grassroots level to raise awareness in minority communities of TB as a critical public health problem. This effort will be challenging because most of the general public views TB as a third-world disease rather than a U.S. problem. ACET can play an important

role in establishing public/private partnerships to frame, deliver and target meaningful, effective and understandable messages to impacted communities.

CDC Perspective. Dr. Hazel Dean, the Associate Director of Health Disparities in the National Center for HIV, STD and TB Prevention (NCHSTP), described disparities in TB rates in the United States. In 2004, 14,511 TB cases were reported in the United States. The total number of cases decreased each year from 1992-2004. Among foreign-born persons, however, the number of TB cases increased from ~5,000 in 1986 to 7,000-8,000 cases each year since 1991. The percentage of TB cases increased from 22% in 1986 to 54% in 2004. The TB rate in 2004 was ~9 times higher compared to U.S.-born persons.

In 2004, 82% of TB cases in the United States occurred in racial/ethnic minority groups with Hispanics and African Americans representing 57% of this burden. Provisional data collected in 2004 showed that Asian/Pacific Islanders (APIs) had the highest TB case rates among all racial/ethnic groups in 1993-2004. The Division of TB Elimination (DTBE) published an article in the *Morbidity and Mortality Weekly Report* (*MMWR*) in July 2004 to describe racial disparities in TB in seven southeastern states. These data showed that 54% of TB cases occurred among African Americans in 2001 in the region compared to 26% in the remainder of the country. In 2002, the TB rate of 11.3/100,000 among non-Hispanic blacks in the region was four times greater than the rate for non-Hispanic whites.

DTBE has undertaken several efforts to address TB racial disparities in the Southeast. Presentations were made to ACET on high TB case rates among African Americans in the Southeast. A call was made for increased TB research and resources. A consultation was convened in May 2003 on TB among racial/ethnic groups in the Southeastern United States. Fact sheets and *The TB Challenge* newsletter on TB disparities are continuing to be developed and distributed. Supplemental funding was awarded to Chicago, Georgia and South Carolina to conduct demonstration projects of innovative strategies to improve TB screening, diagnosis and treatment in high-risk African American communities.

Collaborations were formed with internal CDC partners to apply geographic information system (GIS) data to determine epidemiologic and geographic profiles of TB cases among APIs in the United States. The project is designed to generate information that will assist TB control programs in developing and targeting specific prevention strategies and resources to this population. For example, the GIS data have shown that the disparity in TB rates among APIs is highest in areas with a lower population density. DTBE strongly supports the inclusion of TB as an HHS focus area because this action

will raise awareness in affected communities and facilitate targeted and culturally-relevant prevention strategies.

State Perspective. Dr. Jennifer Flood is an ACET member and the Surveillance and Epidemiology Section Chief of the Tuberculosis Control Branch in the California Department of Health Services. She described TB disparities in California. Of all states, California contributes the most TB cases to the national case burden. TB substantially decreased by ~1,000 cases each year in California in 1995-2000, but the decline of ~300 cases each year in 2000-2005 has not been as significant. Of all TB cases in the state, 76% are among foreign-born persons.

APIs had the largest disparity in California in 1995-2004 with a TB case rate of 28.5/100,000 compared to 1.2/100,000 among whites. Mexico accounts for the majority of the TB epidemiology in the state and contributed 24% of cases in 2004. The decline of TB cases in 1994-2000 among this racial/ethnic group was <50% of U.S.-born cases. Mexico-born TB cases are more likely to be smear-positive and have MDR-TB. Genotyping data suggest 38% of Mexico-born cases result from recent transmission. In a recent case, a smear-positive female 32 years of age arrived to California from Mexico with a long history of multiple TB treatment episodes and extensive cavitary disease. The subject's isolate was resistant to all drugs with the exception of linezolid and para-aminosalicylic acid. The subject is currently infectious, incurable and has two children with skin test conversions.

California treats >100 pediatric TB cases among children <5 years of age each year with Hispanic children accounting for 73% of this burden. Of the pediatric cases, 79% are U.S.-born. In a June 2005 article, the *Oakland Tribune* cited the Urban Institute report that estimated 22% of all American children <6 years of age have immigrant parents; >90% of these children were born in the United States; and nearly 1.3 million live with at least one undocumented parent. Many parents in this minority population fear deportation, present for health care late in the progression of disease or do not seek services to which their U.S.-born children are entitled.

In the San Francisco Bay area, 36% of TB cases have a matching genotype cluster and are the result of recent transmission. Racial/ethnic minority groups were commonly represented in TB outbreak investigations in California from 1998-2004 in various settings, including correctional institutions, dialysis centers, homeless shelters, high schools and workplaces. California is challenged by TB disparities in a number of other areas. Case detection is often difficult in minority groups due to delays in diagnosis and failures in contact investigations.

A field study that defined a “delay in diagnosis” as >6 days from symptom onset found a fair amount of delays in extremely infectious persons. Delays were seen in 40% of sputum smear-positive cases and 43% of cases with cavitary disease. “Patients” or barriers to access to care among racial/ethnic groups accounted for 74% of delays and “providers” accounted for 18% of delays. Preliminary findings of the field study demonstrated a significant association between Asian race and delays. An outbreak of 73 TB cases over a two-year period resulted from a single strain in an urban African American community with a high rate of poverty. Nearly 33% of the cases developed TB due to delayed diagnosis of the source cases. Patients cited fear, stigma, survival needs, lack of transportation, barriers to clinic access, and delays among providers and the health care system as reasons for not initially seeking care.

The number of TB/HIV co-infected cases has increased since 2000, particularly among Hispanics and Asians. The 256 TB deaths reported by the state in 2002 showed disparities among racial/ethnic groups. California acknowledges its substantial social disparities in TB health outcomes, but recognizes that human suffering and community risk can be minimized if TB gaps are addressed. This effort will require national and local recognition.

ACET extensively discussed the issue of TB as a health disparity. From a budget perspective, ACET urged HHS to close gaps in TB health disparities by recognizing the disease as a priority area for funding. Budget cuts in TB control and research will widen gaps in TB rates between minority groups and whites; adversely impact the ability of state and local programs to reach affected communities; and cause delays in promptly intervening in TB transmission. ACET understood Dr. Graham’s clarification that HHS does not maintain a “health disparities list,” but noted the former HHS Secretary generated a list of focus areas for health disparities. Because TB was not included on this list, ACET sent letters in 2003 to the former HHS Secretary and has not received a response to date. Prominent placement and funding of TB will give the disease immediate recognition as a significant health disparity.

From cultural and social perspectives, ACET pointed out that the slower decline of TB, national trends and epidemiology of the disease in California demonstrate cultural issues and other challenges exist in reaching difficult-to-treat communities, such as foreign-born persons and U.S.-born African Americans. TB rates among African Americans in the state of Georgia are eight times higher than those among whites. TB may serve as an entry into these communities because the disease is treatable and curable. Successful treatment of TB and removal of the fear and stigma associated with the disease may improve efforts to address other health disparities of interest to HHS.

ACET made several suggestions for OMH to consider in formally recognizing TB as a health disparity.

- Expand HHS's effective "Take A Loved One To The Doctor Day" media campaign to include TB. Engage media personalities with minority audiences to raise awareness, educate and deliver messages to these communities about TB as a health disparity.
- Encourage OMH to convene a follow-up meeting to the May 2003 consultation on TB among African Americans in the Southeast. Use this event to rejuvenate efforts and revisit commitments made by professional medical societies, CBOs, FBOs and other groups during the consultation. Highlight successful activities and other accomplishments over the past two years.
- Use OMH as a mechanism to strengthen Congressional awareness, support and governmental interest in leveraging resources to recognize TB as a health disparity. Allocate HHS funding for community clinics, health departments and other healthcare providers to deliver culturally-competent TB care. Link funding for Health Resources and Service Administration (HRSA) community health centers (CHCs) to specific TB activities and indicators. Expand HRSA's HIV/AIDS collaborative to include TB.
- Encourage OMH to partner with physician associations that serve African Americans, Hispanics and other minority groups disproportionately impacted by TB. Use these collaborations to encourage physicians to conduct screening and detect clinical signs of TB when patients present for routine care. For example, a consortium of the American Medical Association (AMA), National Hispanic Medical Association and National Medical Association is extremely interested in health disparities and may serve as a valuable partner in delivering effective TB messages to CBOs and grassroots organizations.
- Make a presentation to the HHS Council on the current status of TB health disparities. Cite data, describe lessons learned and highlight evaluation findings from demonstration projects in Chicago, Georgia and South Carolina on innovative strategies to improve TB screening, diagnosis and treatment in high-risk African American communities. Focus on the successes of this effort to leverage new funding for TB control in minority communities.
- Ask the HHS Council to communicate important points to the HHS Secretary. For example, TB should be included on the 500-Day Plan for global priorities. TB will continue to be a problem in the United States

unless strong outreach efforts are made and solid collaborations are developed with the countries of origin of TB patients. TB should be included in the *Surgeon General's Report on Health Disparities* that will be targeted to global issues. HHS should deliver messages to the public to highlight TB as a major health disparity and empower federal agencies and external groups to more effectively conduct activities, raise awareness and build support in diverse sectors.

- Inform HHS that TB is a communicable disease spread by airborne transmission. Emphasize that the public health impact of TB affects both the general public and minority populations and needs special prominence.
- Review HHS's current list of health disparities focus areas to determine if TB can be incorporated into any of these issues. For example, severe cases of pediatric TB that will result in life-long adverse health effects to minority children could perhaps be integrated into the HHS "Closing the Gap" initiative targeted to children.

Dr. Graham formally invited ACET to attend an HHS Council meeting in the near future and make a presentation on TB as a health disparity. He requested that the presentation include effective strategies to engage grassroots communities and other constituents. In terms of scheduling, he conveyed that the HHS Council convenes monthly meetings and ACET could be placed on the July or August 2005 agenda. ACET agreed that Dr. Kawamara will communicate with Dr. Graham to decide on the most compelling topics to include in the presentation and specify expected outcomes of the meeting.

Dr. Walter Williams is the Director of the CDC Office of Health Equity (formerly the Office of Minority Health) and represents CDC on the HHS Council. He planned to relay ACET's suggestions to include TB as a health disparity to the CDC Director. He would particularly highlight CDC's potential role in this effort to enhance education and outreach. Dr. Williams would also notify the CDC Director that specific action items for CDC will most likely be generated from ACET's presentation to the HHS Council.

TB Control and the Role of Primary Care

Ms. Deliana Garcia, of the Migrant Clinicians Network (MCN), described the role of TB control in primary care. The "private sector" that is involved in primary care includes private offices, health centers, prisons, detention centers and all other groups outside of health departments. The major differences between health departments and primary

care settings are as follows. Health departments have a different infrastructure and relationship with patients. The relationship between patients and health departments is terminated after treatment is completed. Health departments have not traditionally integrated services across diseases, are responsible for TB control, and require a thorough understanding of treatment guidelines and access to medication. Primary care settings focus on creating medical homes for persons and engage individuals in preventive, acute and maintenance care.

A decision must now be made on whether primary care providers (PCPs) should provide a limited group of services as determined by the health department or deliver a full array of services required for successful TB control that begins with diagnosis and ends with treatment completion or cure. Funding to supplement infrastructures, communicate with health departments on an ongoing basis and deliver TB services will be needed for PCPs to play an expansive role. The most critical target populations in this effort will be private providers in rural areas who serve migrant or immigrant patients and health centers for migrants, communities and homeless persons. However, these healthcare settings have various structures, focus on different populations, respond to federal, state or local mandates, and operate with funding streams that are different than health departments.

Federally funded health centers comply with mandates established by the HHS Secretary, provide a broad array of health services and respond to community needs. HHS's health disparities focus areas include diabetes, cardiovascular disease, infant mortality, HIV/AIDS, cancer, immunization, depression and asthma. These clinical issues represent the majority of health problems among people of color in low-income, rural or urban communities. Baseline data were collected from these focus areas to monitor progress in the elimination of disparities. The President's Initiative was designed to create 1,200 new and expanded health center access points, impact 1,200 communities by the end of FY'06 and reach an additional six million persons.

Efforts to incorporate TB into these activities will be difficult. TB does not have the same incidence in the U.S. population as the other identified health disparities. TB control is considered to be the responsibility of health departments and the focus on TB will not advance the President's Initiative. However, health departments can take several actions to overcome these barriers. Allies can be created and gaps that have developed over time can be bridged. Health departments can become more visible and vocal, particularly during a TB outbreak, death or other sentinel event.

Effective messages can be delivered at the local level to inform PCPs and the public about the role of the health department in saving lives, preventing further illness and

protecting the public. For example, the likelihood of a lethal case of MDR-TB entering a U.S. community is much greater than an anthrax or smallpox case. Potential carriers of TB disease include workers, students, government officials, tourists, missionaries and other persons who routinely travel between the United States and other countries. Adverse outcomes that will occur without a local public health infrastructure can be highlighted.

Educational and outreach activities at the local level can be targeted to PCPs, such as newspaper editorials, continuing medical education (CME) credits, advisory groups or advocacy committees, open houses at healthcare facilities, and personal experiences described by TB survivors. Ms. Garcia emphasized that primary care is willing and able to become more involved in TB control, but public health must first clearly articulate and define this role.

ACET made several suggestions to strengthen the role of PCPs in TB control.

- Emphasize the critical importance of partnerships between local health centers and health departments in the TB elimination effort. Bridge traditional gaps, minimize barriers and enhance communications between these two groups. For example, the local health center may not have adequate funding and resources to maintain and improve a solid TB infrastructure for bioterrorism issues, administer TB treatment and care, perform x-rays and provide follow-up for latent TB infection (LTBI). The local health department may "blame" the health center for referring TB cases.
- Establish a CDC/ACET collaborative effort to jointly define the role of PCPs in TB control, develop explicit guidelines, leverage sufficient funding and design appropriate educational strategies.
- Use MCN and other organizations to create and distribute position papers and supporting data to the respective memberships about specific actions PCPs can take in TB control at the local level.
- Produce and disseminate "Think TB" buttons and other simple messages to PCPs throughout the country to reiterate the importance of TB control.
- Inform PCPs about existing resources. For example, a user-friendly flip chart with cartoons was recently developed by multiple agencies and organizations to address the importance of managing TB. The educational resource is targeted to providers and patients and will be distributed in both English and Spanish.
- Target groups other than PCPs that play an important role in TB control, such as physicians of osteopathic medicine, academic institution

providers, outreach workers, healthcare organizations, emergency departments, and the newly-formed consortium of medical associations. Urge CDC to assist these groups in formulating TB control implementation strategies that will be realistic and feasible for the particular setting.

CDC made several observations on the role of PCPs in TB control. On the one hand, PCPs can be extensively involved by having a high index of suspicion, promptly diagnosing TB and contributing to targeted testing. On the other hand, PCPs are challenged by maintaining proficiency in TB treatment, drug resistance and other aspects of care because cases present on an infrequent basis. PCPs should retain knowledge about the basics of TB, follow-up actions and available referrals at a minimum.

CDC is currently developing formal guidelines to link PCPs to four Regional Training and Medical Consultation Centers (RTMCCs) to ensure all providers throughout the country have access to TB expertise. CDC is also considering the possibility of developing a list of PCPs who have not been traditionally targeted in TB control, such as pediatricians, family practitioners, physician assistants and nurse practitioners. CDC acknowledges that CME credits for TB courses can be offered during medical conferences and other professional events as an incentive to engage these providers. Moreover, ACET could make a presentation to the American Nurses Association during World TB Day to highlight the critical role of nurses in TB control.

ACET concluded the discussion by agreeing to propose recommendations and concrete action steps with time-lines for the role of PCPs in TB control at a later time during the meeting.

Update by the NCHSTP Acting Director

Dr. Janet Collins covered the following areas in her report. One, the deadline to submit applications for the position of the NCHSTP Director was extended to July 1, 2005. NCHSTP expects to select the new Global AIDS Program (GAP) Director during the summer of 2005 from the final seven candidates identified by the search committee. Two, the tremendous problem of HIV/TB co-infection at the global level was extensively discussed during the GAP annual meeting. Three, the FY'04 "State of CDC" report is posted on the CDC web site and highlights several NCHSTP activities, including the TB genotyping program, TB binational card, GAP initiatives and HIV rapid testing.

Four, CDC will convene the National HIV Prevention Conference on June 12-15, 2005 and the "Public's Health and the Law in the 21st Century" conference on June 13-15, 2005. Both events will be held in Atlanta. Five, CDC's new organizational structure was formally approved by HHS and Congress. Searches are underway to permanently fill senior leadership positions in the Coordinating Center for Infectious Disease (CCID), including the Senior Advisor for Science and Public Health Practice and liaisons to the Office of Workforce and Career Development, Office of Communications and Office of Strategy and Innovation (OSI).

Six, the CCID Director and senior leadership in the three CCID centers attended a retreat in May 2005 to identify roles and responsibilities at the coordinating center, division and center levels and determine if additional reorganization is needed. CCID agreed to systematically assess the strengths and limitations of several organizational models and hold a follow-up retreat by August 2005 to discuss potential changes. Various structures were proposed, such as centralizing senior management authority in CCID; eliminating center directors and appointing deputy directors to report directly to the CCID Director; or maintaining the majority of management responsibilities at the center level. A summary of the May 2005 retreat was distributed to ACET.

DTBE Director's Report

Dr. Kenneth Castro covered the following areas in his report. One, CDC's authorities for TB control include prevention and control services, research on MDR-TB and other TB issues, the TB elimination effort, demonstration projects, public information and education, training to health professionals and ACET activities.

Two, the FY'05 appropriations conference report allocated $2.644 million over FY'04 funding. Congress encouraged CDC to apply a formula, use the increased dollars to maximize the percentage of available TB funds, and ensure no state receives less funds than those allocated in FY'04. Congress also urged CDC to expand efforts to reduce TB racial disparities; continue TB vaccine research; consider screening for LTBI; and improve TB screening, particularly among immigrants from high-burden countries.

CDC must fund its infrastructure, evaluation activities and small business innovation research projects, but will categorically apply future Congressional increases and attempt to protect grantees from internal costs. DTBE's FY'05 budget is $144 million after an 0.8% recission was applied and $19 million was added to support HIV/TB co-infection projects and the Mycobacteriology Laboratory Branch. Of the FY'05 budget, DTBE will allocate $108.25 to TB prevention and control and laboratory activities, $16.7

million to TB research, $4.8 million to international initiatives, and $20.0 to intramural projects. DTBE and the Mexico TB control program are making strong efforts to leverage funding for continued support of the binational TB card project infrastructure.

Three, DTBE published a March 2005 *MMWR* article on TB surveillance data, 2004 U.S. TB trends and information on World TB Day. Four, the Online TB Information System (OTIS) is a public use data set of national TB surveillance data collected in 1993-2003 with 22 variables from the revised verified case TB form. OTIS maintains confidentiality by de-identifying, aggregating or suppressing data; performs queries and ad hoc cross-tabulations; and supplements annual surveillance reports. As of June 2005, three states declined participation in OTIS, delayed its decision or requested suppression of HIV data. The remaining states signed consent forms to participate in OTIS and provide public access to TB surveillance data. States will be given two months to review the OTIS draft, check data, make queries and provide feedback to CDC. OTIS is expected to be released at the end of summer of 2005.

Five, an outbreak investigation team responded to several TB Epi-AID requests in January-May 2005, including Hmong refugees in Thailand and California and TB/HIV co-infected persons in Baltimore. Six, the Tuberculosis Epidemiologic Studies Consortium (TBESC) is focusing on several areas, including immunogenetic markers for susceptibility, pediatric TB, evaluations of HIV in TB contact investigations, LTBI prevalence, TB in foreign-born persons, barriers to adherence to TB treatment, and the molecular epidemiology of MDR-TB.

TBESC is also conducting a variety of activities, such as building regional capacity, analyzing social networks in TB investigations, performing new surveillance evaluations, developing educational materials for Hispanic CBOs, distributing self-evaluations to TB programs, targeting a project to African American women, and administering surveys on the knowledge, attitudes and beliefs of private providers. QuantiFERON-TB (QFT) Gold, Ellispot and nucleic acid amplification tests (NAATs) are TBESC's highest research priorities. However, diagnostic tests are under-funded and DTBE does not anticipate that new dollars will be allocated for TB research. Efforts will be made to redirect funds from studies that are scheduled to be concluded to diagnostic tests and new research activities.

Seven, the Tuberculosis Trials Consortium (TBTC) has completed several studies since 1995. Study 26 is designed to determine whether the currently recommended LTBI regimen of nine months of daily isoniazid (INH) can be shortened to 12 doses. As of June 5, 2005, 4,569 persons of the goal of 8,000 subjects were enrolled. Study 27 is designed as a placebo-controlled and factorial study randomized to analyze drug and

treatment frequency. Preliminary data with 250 subjects did not show statistically significant differences in a two-month culture conversion with moxifloxacin or ethambutol on a daily versus three times a week regimen.

Study 28 will be designed to determine whether replacement of INH with moxifloxacin during an intensive phase will result in a significantly greater proportion of patients whose sputum is culture negative at two months compared to the standard regimen. The primary endpoints of the study will be the proportion of patients with a negative sputum culture after two months of therapy and those who discontinue the assigned study therapy for any reason during the first two months. Persons with resistance to INH or moxifloxacin will be excluded from the study.

Eight, the Federal Bureau of Prisons published a May 2005 *Federal Register* notice to announce that new rules on TB screening and voluntary and involuntary HIV counseling and testing will become effective on June 20, 2005. Nine, efforts to develop and distribute the ACET Foreign-Born Workgroup report have been placed on hold until DTBE completes and releases other guidelines.

In terms of NCHSTP, ACET expressed concerns with the organizational models that were proposed during the CCID retreat. Some of these structures will create new or merge existing divisions, but CDC has not yet demonstrated that its major reorganization at the agency level will benefit local programs. CDC is still in the midst of a tremendous transition and has not permanently filled the majority of leadership positions. Significant changes in or elimination of the current DTBE structure will be extremely detrimental to state and local TB control programs.

In terms of DTBE, ACET suggested that data from TBESC's surveys on the knowledge, attitudes and beliefs of private providers be used to inform efforts on strengthening the role of PCPs in TB control. ACET expressed concern about budget constraints that have resulted in DTBE placing lower priority to important items, such as the ACET Foreign-Born Workgroup report and diagnostic studies.

In response to various questions about CCID organizational structure, it was suggested that ACET communicate with Dr. Mitchell Cohen, the CCID Director, to request data on the proposed organizational models and the rationale for these structures to add value to DTBE. This information will assist ACET in providing informed feedback. Dr. Kawamura agreed to take this action and share Dr. Cohen's response with ACET.

Update on Synergy Between TB Elimination and Emergency Preparedness (EP)

Mr. Charles Schable, Director of the Coordinating Office of Terrorism Preparedness and Emergency Response (COTPER), confirmed his receipt of ACET's November 2004 letter and EP recommendations. He was aware that ACET took this action because EP funding is not applied to TB and opportunities for synergy between the two programs are frequently missed. Moreover, EP typically does not take advantage of the expertise and knowledge of TB control programs in quarantine, law enforcement of TB medications ordered by health officers and other issues.

The Office of Management and Budget and Homeland Security Council (HSC) recently announced that EP dollars can only be used for terrorism preparedness and EP. The order was issued by the White House and is posted on the CDC web site. Although TB is not viewed as a rapid weapon of mass destruction, opportunities are still available to enhance synergy between TB and EP.

TB controllers should be trained in incident command to respond to an event, have knowledge of state and local emergency response plans, and ensure the respective community is incorporated into the plan. TB control staff should participate in tabletop exercises, volunteer for community drills, and take other actions to raise awareness of the critical role of public health in EP. ACET should submit an appeal and supporting data to the appropriate category committee that classifies bioterrorism agents. ACET's request to reclassify MDR-TB as a Category B agent could possibly be completed in six months.

Mr. Schable agreed to provide ACET with contact information for HSC members who have a strong interest in public health issues. He welcomed the opportunity to forward ACET position statements or other documents to HSC and other parts of the federal government. He suggested that ACET rewrite its November 2004 EP recommendations with stronger language to emphasize the critical importance of TB expertise in EP and resubmit the document to COTPER for distribution. However, Mr. Schable cautioned ACET against using the terms "dual use" or "infrastructure" in its communications because Congressional funds were only appropriated for EP, emergency response and terrorism activities.

ACET asked COTPER to consider the following recommendations to increase the synergy between TB and EP.

- Use EP dollars to support full-time positions in TB control programs. Provide a clear rationale for removing staff from communicable disease programs to new EP programs in state and local health departments.
- Incorporate explicit TB language into CDC's new five-year cycle of EP grants that will be awarded to state health departments. Structure grant language to allow full use of EP dollars and provide more flexibility to state and local health departments. For example, emphasize the fact that the expertise of TB control programs in airborne diseases, isolation, contact investigations and disease control is more than sufficient to address anthrax and other areas in terrorism preparedness and emergency response.
- Urge the CDC Director to allocate EP dollars to NCHSTP and other centers with expertise in emergency response, laboratory science and environmental effects.
- Explore the possibility of applying funds from the Early Warning Infectious Disease Surveillance project that are available to 20 border states to strengthen the capacity of TB management.
- Use TB outbreaks in EP tabletop exercises.
- Collaborate with ACET to make CDC leadership aware of skill sets shared by TB and EP. Emphasize the fact that efforts to strengthen one system will benefit the other.

ACET moved to submit an appeal to reclassify MDR-TB as a Category B bioterrorism agent. The motion was properly placed on the floor, seconded by voting members and **unanimously approved** with no further discussion.

ACET agreed to take the following actions to advance this effort. Dr. Fleenor and Ms. Napolitano will revise ACET's November 2004 EP recommendations. Dr. Flood and Ms. Stricof will draft language for ACET's motion to reclassify MDR-TB as a Category B agent. DTBE will provide the writing groups with appropriate language to revise the EP recommendations and specific criteria that are used to classify agents. DTBE will distribute the motion and revised recommendations to ACET by e-mail for review, comment and a formal vote. COTPER will ask DTBE to identify internal and external subject matter experts who should participate in the decision-making process to reclassify MDR-TB as a Category B agent.

Update on QFT-Gold Guidelines

Dr. Andrew Vernon of DTBE provided a status report on CDC's process to develop the QFT-Gold guidelines. CDC published an *MMWR* article in January 2003 with guidelines for the first generation of QFT 15 months after a Food and Drug Administration (FDA) panel recommended approval. FDA granted preliminary approval of QFT-Gold as a diagnostic aid in December 2004. The application served as a supplement to approval of the original QFT test and did not require a panel process. FDA granted final approval of QFT-Gold in March 2005 after receiving responses from the manufacturer to outstanding questions. FDA is currently considering the manufacturer's proposal to modify the calibration curve.

CDC considered several issues while preparing the QFT-Gold guidelines, such as the ability of the test to predict progression to TB; the predictive capacity of the test compared to the tuberculin skin test; the accuracy of the test in children, HIV-infected persons or immunocompromised patients; the appropriate setting and process to implement testing; and the need for post-marketing data on the performance and economic impact of QFT-Gold. CDC drafted the QFT-Gold guidelines and convened a group of experts in May 2005 to discuss concerns and share pre-publication data.

CDC then convened an informal ad hoc consultation with additional experts to review presentations of existing and new data. The experts were asked to consider four questions. First, should CDC convene a formal expert consultation to review data and recommend key elements of the QFT-Gold guidelines? Second, if not, should CDC include restrictions on the recommended use of QFT-Gold in contacts, children <5 years of age, healthcare workers and immunosuppressed persons? Third, should the guidelines offer general observations and note specific groups or circumstances where data are not available for CDC to recommend for or against the use of QFT-Gold? Fourth, should CDC request and plan for Phase 4 surveillance and for which events?

In response to unanimous agreement during the ad hoc consultation, CDC will convene a meeting with ACET members, investigators and other subject matter experts on July 11-12, 2005 to review data, attempt to answer outstanding questions and make recommendations on the QFT-Gold guidelines. The final guidelines will be posted on the DTBE web site and a "Notice to Readers" will be published in the *MMWR*. Dr. Vernon agreed with ACET's comment that data were not presented during the update, but CDC has not been granted approval to publicly share manufacturer data and pre-publication reports at this time.

CDC's Draft TB Infection Control Guidelines

Dr. Dixie Snider, the Chief Science Officer, joined the meeting to discuss CDC's upcoming publication of the draft guidelines. He sent a letter to Dr. Kawamura dated June 2, 2005 in response to ACET's March 10, 2005 letter on this issue. His comments on the current status of the guidelines are as follows. The *MMWR* is currently editing the document, but cannot make substantive changes without approval from DTBE, the National Center for Infectious Diseases and the National Institute for Occupational Safety and Health (NIOSH).

The most significant changes in the guidelines are as follows. Language on the scope of healthcare settings was expanded to include laboratories and additional outpatient settings. Risk assessment approaches were updated to reflect more recent epidemiologic trends and circumstances in healthcare settings that have occurred over the past ten years. Recommendations on annual respirator training, initial and periodic fit testing, and respirator performance specifications were included, but this guidance is the most controversial area of the guidelines.

Many participants at CDC's stakeholders' workshop on respiratory protection for airborne infectious agents on November 30-December 1, 2004 expressed concerns and conflicting views about the guidelines. On the one hand, data are insufficient to make evidence-based recommendations on respirator performance specifications and the periodicity of fit testing. On the other hand, the guidelines should be flexible and include effective and practical interventions other than respiratory protection for settings with limited infection control resources. Minimum respirator performance should be specified, such as "the respirator design should provide a good fit for at least 95% of persons tested."

CDC considered all perspectives and decided to include the following language in the guidelines. Initial and periodic fit testing is recommended. The periodicity is not specified; instead, a referral is made to Occupational Safety and Health Administration (OSHA) regulations for annual fit testing. Decisions on the frequency of periodic fit testing should be supplemented by local data, such as the risk of transmission of *Mycobacterium tuberculosis* (*M.tb*); facial features, medical conditions and other characteristics of the individual that may affect respiratory function; and model size and other characteristics of the respirator.

The process of selecting respirators may be informed through consultation with respirator fit testing experts, CDC, occupational health and infection control professional organizations, peer-reviewed research, respirator manufacturers or advanced respirator

training courses. CDC acknowledges that additional science must be generated to produce stronger and more definitive recommendations on TB infection control. CDC will continue to leverage additional resources for more research to fill existing scientific gaps.

Dr. Snider responded to ACET's specific questions as follows. First, the Office of the Chief of Science has requested that several important topics be flagged for inclusion in the CDC-wide research agenda. Issues of relevance to ACET include the efficacy of masks and respirators in preventing transmission of microorganisms; the contribution of fit testing and respirators to healthcare worker protection; and the relative importance of respirators in preventing transmission of infectious diseases compared to other control measures in a personal protective equipment (PPE) program.

CDC will continue to gather public comments and other input to identify priorities for the research agenda. For example, efforts could be made to incorporate respiratory protection into a larger thematic area and then leverage funds to support this broader issue. CDC is extremely pleased that advocates, constituents and other external groups have made a commitment to use the research agenda to expand CDC's intramural and extramural research portfolio.

Second, CDC could not take action on ACET's recommendation to remove all references to OSHA from the guidelines because OSHA has regulatory and legal authority for respiratory protection. However, the guidelines encourage risk-based assessments for appropriate decisions in particular settings and does not recommend a "standard" regulatory approach.

Third, ACET should build a relationship with and engage OSI in ongoing dialogue. These discussions could focus on the incorporation of TB research into the CDC-wide research agenda, the process to prioritize research topics, and approaches to leverage funding for DTBE to further study QFT-Gold. OSI is responsible for establishing CDC's health protection goals, identifying objectives and strategies for each goal, and redirecting administrative savings to programs. OSI will use health burden and other specific criteria to determine CDC's funding priorities and future direction. Because OSI is using an open and transparent process to develop criteria, opportunities are available for ACET to provide input at this time. For example, TB will play a critical role in CDC's global health goals.

ACET's recommendations to CDC are outlined below.

- Base the TB infection control guidelines on actual experiences over the past ten years. For example, CDC's 1994 guidelines did not recommend initial, periodic or annual fit testing. Adherence to this guidance resulted in TB control in healthcare facilities without annual fit testing. As a result, the scientific rationale of OSHA's annual fit testing requirement is uncertain. NIOSH studies conducted by trained investigators in controlled laboratory settings did not show any fit testing method that was reliable or reproducible. Based on these data, the infection control community will face significant staff and resource constraints to implement OSHA's labor-intensive respiratory protection regulations and adhere to CDC's revised guidelines.
- Partner with regulatory agencies to require manufacturers to develop inherently good fitting respirators out of the box.
- Immediately provide infection control programs with explicit advice to implement the TB infection control guidelines. For example, CDC's guidance to review OSHA's respiratory protection regulations and conduct a risk assessment conflicts.
- Add a cost-benefit ratio study to CDC's list of research agenda priorities to determine cost savings from the number of TB infections or cases averted with a PPE program.

With no further discussion or business brought before ACET, Dr. Kawamura recessed the meeting at 5:03 p.m. on June 8, 2005.

Current ACET Business

Dr. Kawamura reconvened the meeting at 8:39 a.m. on June 9, 2005 and entertained a motion to accept the previous meeting minutes. The motion was properly made and seconded by voting members. The February 16-17, 2005 ACET Meeting Minutes were **unanimously approved** with no changes or further discussion.

ACET's suggestions of items to add to the ongoing list of future agenda topics are outlined below.

- Update by DTBE on the agenda and future plans of RTMCCs.
- Report by the U.S.-Mexico Border Health Commission on Binational Health Week.
- Report by OSI on actions taken to incorporate the TB elimination effort into the CDC-wide research agenda.

- Update by DTBE on the use of automation in local data reporting systems for TB surveillance.
- Overview by DTBE or the Division of Global Migration and Quarantine (DGMQ) on infection control practices in Canada, Taiwan and other developed countries outside of the United States.
- Update by the National Institutes of Health on TB vaccine research activities.

Update on TB in Recently Resettled Hmong Refugees

Dr. Castro reported that the Royal Thai government requested U.S. resettlement of 15,000 Hmong refugees in January 2004 due to the closing of the Wat Tham Krabok camp near Bangkok. Because of enhanced screening in June 2004 with *M.tb* cultures and drug susceptibility testing (DST), four adult MDR-TB cases were reported. In June 2004-January 2005, ~9,500 Hmong refugees settled in 27 states with 75% arriving in California, Minnesota and Wisconsin. CDC received reports from California of TB and MDR-TB cases in recently resettled Hmong refugees 4-71 years of age and learned of 13 additional MDR-TB cases in refugees in Thailand.

Several actions were taken in response to these reports. CDC requested an immediate halt to further resettlement until refugees in the Wat Tham Krabok camp were re-screened. CDC recommended that the time period between evaluation and travel be shortened to one month. A federal interagency task force was established to develop updated overseas TB screening and treatment protocols to include the screening of children <15 years of age. States, refugee programs and Hmong communities in the United States were notified of the revised protocols. CDC provided epidemiologic assistance to California and Thailand.

The investigation at the Wat Tham Krabok camp resulted in an estimated TB rate of 1,780/100,000 and confirmation of 17 MDR-TB cases. Infection control measures included case management, contact tracing and health education campaigns. Factors that contributed to the high incidence of TB among refugees included crowded living conditions, lack of respiratory isolation and delayed TB diagnoses. TB in children, MDR-TB and culture-positive/smear negative TB cases were overlooked due to flawed screening protocols and the lack of cultures.

As of June 2, 2005, CDC received reports of 37 TB cases in recently resettled Hmong refugees with seven cases in children <5 years of age, two cases deemed to be suspects, and four cases confirmed with MDR-TB. To date, 427 contacts have been

investigated. CDC provided onsite epidemiologic support to two counties in California to review the cases in detail, determine epidemiology links and develop a database to track contacts. The rate in California was estimated to be 837/100,000 in Hmong refugees compared to 391/100,000 in the remainder of the United States.

CDC learned of several obstacles during the field investigation. Large Hmong families and close-knit communities facilitate transmission and increase the difficulty of investigations. Consistent messages must be delivered and culturally-sensitive models must be developed to promote TB awareness and education. Language barriers, cultural differences, challenges with asymptomatic patients who experience side effects with TB medication, and lack of trust of public health authorities must be overcome.

Programmatic challenges include difficulties in making linkages and tracking contacts across jurisdictions; inaccurate identification of persons due to similar names or alternate spellings; individuals with missing or incomplete demographic data, such as date of birth or addresses; and the establishment of new collaborations between refugee health and TB programs. Other challenges include the exclusion of healthcare costs in the Department of State (DOS) budget. Screening and treatment programs are poor, laboratory quality and capacity are limited, public health resources are insufficient, and national notification and follow-up of cases are inadequate. CDC is aware of the critical need to address these challenges because ~140,000 Burmese refugees are scheduled for U.S. resettlement over the next few years.

CDC staff were detailed to Thailand to provide technical assistance for case management of MDR-TB. Ongoing contact investigations have shown transmission within family clusters, but have not produced evidence of new cases. Several actions were taken to improve initiation, completion and evaluation of treatment in both Thailand and the United States at local, state, national and international levels. The screening process was streamlined, more interpreters were hired, and culturally-appropriate education strategies were implemented. Consultations, onsite support and funding were provided and briefings were presented to CDC leadership.

CDC will continue to improve collaborations between refugee health and TB programs. States and CDC will continue to provide support for contact investigations, the development of databases, and education and outreach campaigns. Partnerships will be established with leaders in Hmong communities. A briefing will be presented to HHS in July 2005 and an *MMWR* report is currently undergoing the clearance process.

The investigation of TB in recently resettled Hmong refugees resulted in CDC making several recommendations. Comprehensive diagnostic and case management should

be implemented for TB and MDR-TB. DST and laboratory capacity should be enhanced overseas. A national electronic notification and follow-up system should be implemented. Insurance should be offered for MDR-TB treatment. State and local public health response capacity should be supported. A DGMQ staff member should be assigned to Asia. TB screening and treatment practices should be evaluated and expanded overseas. A formal DOS/HHS task force should be established to specifically focus on refugee resettlement and immediately notify CDC of resettlement decisions. Per capita costs should be reassessed and resources should be identified for the DOS/HHS task force.

ACET commended CDC for deploying a team to Thailand, rapidly responding to Hmong TB cases in the United States, and providing epidemiologic assistance to California. However, some members were extremely concerned that the federal government has not developed a concrete plan to ensure a similar situation does not occur in the future. Increases in TB and MDR-TB in the United States due to recently resettled Hmong refugees could have been predicted and entirely avoided if the U.S. government had immediately notified CDC and other public health agencies of the arrival of these persons.

ACET acknowledged that the problem also could have been prevented by providing sufficient resources for quarantine stations to thoroughly screen and evaluate refugees and immigrants and allocating funds to strengthen laboratory capacity in the respective countries of origin. These failures have placed citizens in the 27 states at risk and further emphasize the need to build relationships between TB and EP infrastructures. ACET pointed out that TB in Hmong refugees serves as a solid example to include TB treatment in the President's Emergency Plan For AIDS Relief and other overseas initiatives.

ACET asked CDC to consider the following recommendations.

- Maintain a five-member CDC team in Thailand for at least two years, including a physician and nurse. Use this strategy to facilitate programmatic support and implement changes in screening, culture sensitivity and other policies overseas. Make solid recommendations on changes in overseas policies and associated costs. Present a status report during the next ACET meeting on policies, resources, actions and costs related to immigration screening and international investments for TB control.
- Invite DOS to make a presentation during the next ACET meeting on future plans to address refugee resettlement issues. Ask Mr. Schable to

attend the meeting to offer guidance on using this opportunity to enhance synergy between TB and EP.

- Collaborate with HRSA to widely distribute notices to alert CHCs, emergency departments and private providers throughout the country that Hmong refugees may present for TB treatment.

DTBE's Diagnostic Activities

Dr. Thomas Shinnick of DTBE reported that DTBE is conducting several diagnostic activities in response to the Institute of Medicine report, *Ending Neglect*. For the goals of maintaining control and accelerating the decline of TB, DTBE is developing new tools for epidemiologic studies, such as strain typing methods for *M.tb* and the identification of infection and disease markers. Operational research is being performed to design testing algorithms and create manuals to interpret results. For the goal of developing new tools, DTBE established the TBESC infrastructure for diagnostic studies; evaluated tests for LTBI and TB disease; created new laboratory-based tests; and implemented operational and translational research.

QFT and Ellispot are being used to analyze the prevalence of LTBI among high-risk populations in the United States. Diagnostic tests for active TB disease include the TB patch test, sero-diagnostic tests for pediatric TB, low-cost rapid media, improved acid fast bacilli smear microscopy, and NAATs to detect *M.tb*, predict relapse and monitor treatment. DTBE considers NAAT-based tests to be the state-of-the-art for laboratories with no resource limitations. These tools should have capacity to detect *M.tb* from a sputum specimen, generate results to clinicians within 24-48 hours, and produce results on rifampin resistance or susceptibility within the same time period. DTBE will complete its review of the NAAT guidelines after the QFT-Gold guidelines are published.

A large prospective contact investigation study is underway in DTBE that focuses on host genetic factors to identify potential markers of TB infection or disease and blood-based assays. Laboratory-based tests are ongoing to determine typing methods for *M.tb* and non-tuberculous mycobacteria, methods to identify species, and genotypic and phenotypic DSTs. Operational and translational research is being performed to assess new testing algorithms; develop strategies to improve laboratory services in the United States; and identify the cost effectiveness and benefits to TB control programs and individual patients of NAAT-based tests, rapid liquid culture methods and rapid diagnosis of MDR-TB. DTBE published an *MMWR* article in April 2005 to describe components that will be needed to improve laboratory services in the United States.

In 2004-2005, DTBE compiled and reviewed a catalogue of its diagnostic research activities; identified the need to evaluate projects and establish priorities; and designed a concept to manage the portfolio. This effort resulted in DTBE proposing three diagnostic workgroups. The Diagnostics Lead Workgroup will be represented by DTBE senior leadership to oversee diagnostic activities, address resource issues and make recommendations to the DTBE Director on diagnostic activities and priorities. The Internal Diagnostics Workgroup will be represented by DTBE division, branch and program staff to define DTBE's role in test development; draft and review DTBE diagnostic priorities; review the science; determine the focus, objectives, progress and time-lines of projects; identify overlapping areas; and promote synergies.

The internal group will be charged with focusing on specific issues, such as CDC's unique role in test development, limitations to CDC's activities, the needs and time-lines of CDC's TB diagnostic priorities, balance in the diagnostics portfolio, and opportunities for coordination and collaboration. The External Diagnostics Workgroup will be represented by the TBESC workgroup, a variety of federal partners and diverse non-governmental organizations to provide input on CDC priorities, propose projects to address CDC research priority needs, identify strategic opportunities, and assist in incorporating CDC activities into domestic and international diagnostic activities.

ACET commended DTBE on its outstanding efforts to test new diagnostics and perform operational research in the field. Several members made suggestions for DTBE to consider during further development of its TB diagnostics research portfolio.

- Continue to focus on LTBI diagnosis as a priority in the TB elimination effort.
- Acknowledge the critical importance of diagnostic tools to enhance rapid diagnosis of susceptibility, particularly with the increased global prevalence of MDR-TB.
- Apply and evaluate TB diagnostic tools in Hmong refugees. Obtain and assess specimens and prospectively follow this population over time to strengthen laboratory studies and other components of the TB diagnostics research portfolio.
- Leverage funding to conduct operational research and assess the availability of NAAT through state laboratories.
- Make DST available as a rapid first line-agent as moxifloxacin and quinolones become first-line agents.

Update on TB Vaccine Regulatory Issues

Dr. Sheldon Morris, the ACET *ex officio* member for FDA, provided a status report on regulatory issues associated with the clinical development of new TB vaccines. Three clinical trials are underway for new TB vaccines. Phase I tests were completed and FDA approved testing for the recombinant BCG expressing antigen 85 and a protein subunit vaccine with a GlaxoSmithKline adjuvant. A modified Vaccinia virus construct expressing antigen 85A was tested in the United Kingdom in Phase I testing. A recombinant BCG expressing listeriolysin, fusion protein subunit vaccine with an adjuvant, and adenoviral constructs to boost BCG responses are scheduled to be tested in 2006. Recombinant BCG and live attenuated vaccines will induce a PPD response. Several sponsors are attempting to develop vaccines that do not convert to a tuberculin reaction.

FDA is addressing several regulatory issues related to different types of TB vaccines. The effectiveness of recombinant BCG may be minimized by environmental mycobacterial exposure. Protein subunit vaccines with an adjuvant have tremendous toxicity. DNA vaccines have problems integrating with chromosomes. Viral vectored vaccines contain preexisting antibodies to the virus. Live attenuated strains have the potential for reversion. FDA is also challenged by different indications of TB vaccines, such as the prevention of TB dissemination, re-infection and infection in infants and adults; control of LTBI and TB in HIV-infected persons; the boost from BCG responses; and adjuncts to chemotherapy in persons with active disease. Different types of clinical trials with various sizes and endpoints will need to be designed to address these issues.

Another significant concern is different study populations, including BCG-vaccinated persons; patients with LTBI, HIV infection or active TB disease; and infants, children, adults and other non-immune individuals. Factors associated with TB/HIV co-infection must also be considered in study populations, such as concerns with the use of live vaccines in immunocompromised hosts, the ability of immunocompromised hosts to mount immune responses, and the potential for HIV subjects to have atypical presentations of active TB disease. FDA must answer three major questions to maintain its first priority of safety in study populations. First, can FDA safely proceed to clinical testing in highly endemic areas with data only from persons living in non-endemic regions? Second, what safety and efficacy data are required prior to enrolling infants? Third, what data are required prior to studying a new TB vaccine in an HIV-positive population?

LTBI screening is an additional regulatory issue because the current policy states that only FDA-approved diagnostic reagents can be used in clinical trials. Efforts are being

made to change this policy. Immunization of LTBI patients causes safety concerns because recent animal studies have shown worsening lung pathology after TB vaccine injections. Pre-clinical tests are being designed to assess the safety of post-exposure immunization. Primary endpoints are problematic in vaccine clinical trials as well. TB case definitions can vary globally and disease is difficult to detect in infants. HIV-positive patients may present diagnostic changes and no correlates of protective immunity currently exist.

Clinical trials outside the United States are difficult because FDA has no authority to regulate products for use in these settings and non-licensed diagnostic products are often used in international trials. FDA has not designed a formal mechanism to provide guidance to developing countries. Different benefit-risk ratios increase the difficulty of regulating products for use in non-U.S. populations. Equivalence to the licensed product must be demonstrated before a new vaccine can be licensed, but FDA is currently attempting to develop a waiver to this regulation. Non-U.S. clinical trials have different standards for health care, informed consent, monitoring procedures, source documentation, laboratory capacity, reporting of adverse events, and logistics for vaccine delivery and storage.

Regulatory issues associated with BCG include the ethics of withholding the vaccine, the questionable efficacy of BCG, the use of different strains and methods of administration at the global level, and impacts on the design, size and blinding of clinical trials. FDA will also face challenges with clinical trials in the United States because U.S. bridging studies will be required, but cannot be successfully completed in the absence of correlates of immunity. The ability to conduct Phase II or III efficacy studies for a TB vaccine in the United States has not yet been determined. The U.S. indication for a TB vaccine has also not been specified.

These important regulatory issues must be resolved prior to Phase III testing and eventual licensure of new TB vaccines. However, five to ten new TB vaccines will most likely be evaluated in clinical trials in the next two to three years. FDA is requesting input from CDC and other public health agencies on identifying the best U.S. and global settings for TB vaccine testing. FDA is also asking the public health community to assist sponsors in addressing clinical health issues.

Public Comment Period

The Chair opened the floor for public comments; no attendees responded.

New ACET Business

Dr. Kawamura asked DTBE to use mathematical modeling to answer the following question and provide a response at a future ACET meeting. At what point would a dominant strain of MDR-TB be developed in a population with "X%" INH drug resistance and use of the World Health Organization diagnosis and treatment regimen of six months of the standard therapy? ACET agreed that Dr. Sally Blower should be invited to a future meeting to present MDR-TB modeling data she has collected.

Dr. Kawamura returned the discussion to ACET's agreement on the previous day to make recommendations and specify concrete action steps with time-lines on the role of PCPs in TB control. ACET's suggestions to advance this effort are outlined below.

- Collaborate with ACET's AMA liaison to compile a list of primary care organizations to target in outreach efforts, particularly medical societies that serve minority populations.
- Develop and widely disseminate an ACET statement about the role of PCPs in TB control during World TB Day. Engage the American Academy of Pediatrics, American Academy of Family Practice and American College of Physicians to post links to World TB Day and notices about the ACET statement on the respective web pages. Urge all ACET liaisons to further distribute the statement through their organizational newsletters and web sites. Ask each professional society to track the number of hits on the TB web page or link.
- Encourage DTBE to sponsor a TB web-cast.
- Inventory existing TB courses and information that would be relevant to PCPs and offer CME credits. Include *MMWR* summary reports in this effort.
- Publish a TB article and ACET commentary in *Annals of Internal Medicine* and an *MMWR* article with TB statistics on World TB Day.
- Take advantage of grand rounds and other existing opportunities in hospitals and health departments. For example, infection control practitioners and epidemiologists will assist hospitals and health departments in conducting risk assessments to support CDC's TB infection control guidelines. TB presentations could be incorporated during regular hospital staff meetings in areas with a high TB burden.
- Redesign HHS's national "Take A Loved One To The Doctor Day" media campaign as local initiatives that specifically focuses on TB. Establish local advisory groups to promote the campaign. Distribute letters to

potential partners to obtain commitments, particularly the local news media, health departments and hospitals.

- Charge RTMCCs with the following tasks. First, compile and widely distribute a list of health department services and other resources to ensure PCPs, nurses, outreach workers and other providers retain a minimum skill set of diagnosing TB. Second, gather a series of compelling case studies and disseminate these data to professional organizations for presentation to respective memberships. Third, partner with state and local health departments to identify PCPs and patient populations in the respective areas and collect information that is relevant to the local jurisdiction.
- Review lessons learned and successes of previous efforts. For example, ask professional organizations that participated in the National TB Training Initiative and developed the first TB core curriculum to share experiences in widely disseminating messages to constituents.
- Partner with the American Public Health Association, National Commission on Correctional Health Care, National Health Care for the Homeless Council, and Society for Correctional Physicians to reach providers who are members of these groups.
- Determine whether funding and resources can be leveraged to sample memberships of the respective professional organizations and evaluate changes in TB knowledge, attitudes, beliefs or practices. Ask DTBE to establish a baseline target, indicator or objective to measure success of outreach efforts to PCPs.
- Use existing opportunities to obtain feedback from PCPs. For example, RTMCCs will conduct a needs assessment over the next few months by administering key informant interviews and surveys to PCPs. Questions to PCPs about the most effective and important messages, materials and educational resources could be included in the questionnaires.

ACET concluded the discussion by agreeing to take the following actions. The preliminary communications plan for World TB Day will be presented at the next agenda. Dr. Kawamura will draft ACET's statement on the role of PCPs in TB control and distribute the document by e-mail to the full membership for review and comment prior to the next meeting. She will also contact ACET's AMA liaison to request assistance in compiling a list of professional organizations and formulating an effective dissemination strategy. The issue of evaluating outreach efforts to PCPs will be discussed in more detail during the next meeting.

Closing Session

The next ACET meeting will be held on November 16-17, 2005. With no further discussion or business brought before ACET, Dr. Kawamura adjourned the meeting at 11:51 a.m. on June 9, 2005.

I hereby certify that to the best of my knowledge, the foregoing Minutes of the proceedings are accurate and complete.

_____
Date

_____
L. Masae Kawamura, M.D.
ACET Chair

ATTACHMENT 1

List of Participants

ACET Members
Dr. Masae Kawamura, Chair
Dr. Jeffrey Douglas
Dr. Michael Fleenor
Dr. Jennifer Flood
Dr. Richard Fluck
Ms. Sara Loaiza
Ms. Eileen Napolitano

***Ex Officio*s and Liaisons**
Dr. William Baine (AHRQ)
Dr. Henry Blumberg (IDSA)
Dr. Garth Graham (HHS/OMH)
Dr. Gail Jacobs (NIH/NIAID)
Dr. Sheldon Morris (FDA)
Ms. Eva Moya (U.S.-Mexico BHC)
Dr. Michael Puisis (NCCHC)
Dr. Gary Roselle (VA)
Dr. Diana Schneider (DIHS)
Ms. Rachel Stricof (APIC)
Dr. Theresa Watkins-Bryant (HRSA)
Dr. David Weissman (NIOSH)

Designated Federal Official
Dr. Ronald Valdiserri,
Executive Secretary

CDC Representatives
Dr. Janet Collins
(NCHSTP Acting Director)
Dr. Kenneth Castro (DTBE Director)
Ms. Susana Calderon
Ms. Ann Cronin
Dr. Hazel Dean
Ms. Heather Duncan
Ms. Mollie Ergle (Contractor)
Ms. Paulette Ford-Knights
Mr. Michael Fraser
Dr. Maryam Haddad
Mr. Dale Hu
Dr. Paul Jensen
Dr. John Jereb
Ms. Erin Lewis
Ms. Suzanne Marks
Dr. Jerry Mazurek
Dr. Scott McCoy
Dr. Mary Naughton
Dr. Adelisa Panlilio
Mr. Scott Santibanez
Mr. Charles Schable
Ms. Margie Scott-Cseh
Dr. Thomas Shinnick
Dr. Dixie Snider
Ms. Brooke Steele
Dr. Phillip Talboy
Dr. Zachary Taylor
Dr. Andrew Vernon
Dr. Walter Williams

Guests
Ms. Patryce Curtis
(The MayaTech Corp.)
Dr. Edward Ellis
(Public Health Agency of Canada)
Ms. Deliana Garcia
(Migrant Clinicians Network)
Ms. Carol Pozsik (NTCA)
Mr. John Seggerson (NCET)
Mr. Anthony Tran (Association of
Public Health Laboratories)
[via conference call]